



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/621,254	07/14/2003	Steven W. Dow	JUVARIS1120	9736
28213	7590	01/09/2009	EXAMINER	
DLA PIPER LLP (US) 4365 EXECUTIVE DRIVE SUITE 1100 SAN DIEGO, CA 92121-2133			HOLLERAN, ANNE L	
			ART UNIT	PAPER NUMBER
			1643	
			MAIL DATE	DELIVERY MODE
			01/09/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/621,254

Applicant(s)

DOW ET AL.

Examiner

ANNE L. HOLLERAN

Art Unit

1643

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 September 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) See Continuation Sheet is/are pending in the application.
- 4a) Of the above claim(s) 8, 19, 39, 43-45, 47, 50-52 and 157 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7, 10, 31-33, 35, 36, 40, 42, 55-68, 85-87, 112-119 and 152-156 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-946)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 9/2008
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date: _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

Continuation of Disposition of Claims: Claims pending in the application are 1-8,10,19,31-33,35,36,39,40,42-45,47,50-52,55-68,85-87,112-119 and 152-157.

DETAILED ACTION

The amendment filed September 12, 2008 is acknowledged.

Claims 1-8, 10, 19, 31-33, 35, 36, 39, 40, 42-45, 47, 50-52, 55-68, 85-87, 112-119, and 152-157 are pending.

Claims 8, 19, and 157 drawn to non-elected inventions, are withdrawn from consideration.

Additionally, claims 39 and 43-45, 47 and 50-52, dependent from canceled claim 34, are objected to for depending from a canceled claim, and are WITHDRAWN from consideration.

Claims **1-7, 10, 31-33, 35, 36, 40, 42, 55-68, 85-87, 112-119, and 152-156** are examined on the merits.

Information Disclosure Statement

With respect to references “JP” to “BBL”, the information disclosure statement filed 9/19/2008 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. References “JP” through “BBL” have not been considered.

Claim Rejections Withdrawn:

The rejection of claims 1-7, 10, 31-36, 38-40, 42-45, 47, 50-52, 55-68, 85-87, 112-121, 152-156 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of treatment of a subject with cancer comprising administering a composition comprising a pattern recognition receptor ligand and a delivery vehicle comprising a liposome, where the liposome is a positively charged liposome, does not reasonably provide enablement for methods comprising the administration of a composition comprising a pattern recognition receptor ligand and a delivery vehicle comprising a liposome where the liposome is a neutral liposome or a negatively charged liposome, is withdrawn in view of the amendment to the claims limiting the liposome to a positively charged liposome.

The rejection of claims 1-7, 10, 31-36, 39, 40, 42, 43-44, 61, 64, 65, 85-87, 112, 118, 120, 151, and 156 under 35 U.S.C. 103(a) as being obvious over Dow (US 6,693,086; issued Feb. 17, 2004; effective filing date, June 25, 1998) in view of Milas (supra) is withdrawn.

The declaration under 37 CFR 1.132 filed 9/12/2008 is sufficient to overcome the rejection of claims 1-7, 10, 31-36, 39, 40, 42, 43-44, 61, 64, 65, 85-87, 112, 118, 120, 151, and 156 based upon the rejection under 35 USC 103(a) as being obvious over Dow in view of Milas.

Claim Rejections Maintained and New Grounds of Rejection:

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined claim(s) is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-7, 10, 19, and 85-87 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 47-54 of copending Application No. 11/320,019. Although the conflicting claims are not identical, they are not patentably distinct from each other because the methods claimed in 11/320,019 anticipate the methods of claims 1-7, 10, 19 and 85-87, which no longer recite a step of administering radiation therapy. Thus, the methods of copending application 11/320,019 recite all the limitations of claims 1-7, 10, 19 and 85-87 of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 31-33, 35, 36, 40, 42, 55-68, 112-119 and 152-156 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 47-54 of copending Application No. 11/320,019 in view of Milas (Milas, L., Develop. Biol.

Standard., 38: 301-306, 1978. The methods of copending Application No. 11/320,019 are drawn to method comprising administering to a mammal a cationic liposome delivery vehicle and an isolated bacterially-derived nucleic acid vector without a gene insert, or a fragment thereof (which is a ligand for a pattern recognition receptor). The methods do not recite a step of administering radiation therapy. However, Milas teaches combining an immunotherapeutic method with radiation therapy to increase the effectiveness of an immunotherapeutic method. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the methods of copending Application No. 11/320,019 to stimulate the immune system and to combine this method with radiation therapy as taught by Milas. One would have been motivated by the teachings of Milas that methods of treating cancer by immunotherapy may be enhanced by combining them with radiation therapy.

This is a provisional obviousness-type double patenting rejection.

Claims 1-7, 10, 19, and 85-87 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 7-20, 24-31, 50-53, 66 and 67 of copending Application No. 10/772,913. Although the conflicting claims are not identical, they are not patentably distinct from each other because the methods claimed in 10/772,913 anticipate the methods of claims 1-7, 10, 19 and 85-87, which no longer recite a step of administering radiation therapy. Thus, the methods of copending application 10/772,913 recite all the limitations of claims 1-7, 10, 19 and 85-87 of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 31-33, 35, 36, 40, 42, 55-68, 112-119 and 152-156 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 7-20, 24-31, 50-53, 66 and 67 of copending Application No. 10/772,913 in view of Milas (Milas, L., Develop. Biol. Standard., 38: 301-306, 1978. The methods of copending Application No. 10/772,913 are drawn to method comprising administering to a mammal a liposome delivery vehicle (which may be cationic liposomes, see claim 14) and total RNA isolated from a tumor sample, said RNA encoding tumor antigens (which is a ligand for a pattern recognition receptor). The methods do not recite a step of administering radiation therapy. However, Milas teaches combining an immunotherapeutic method with radiation therapy to increase the effectiveness of an immunotherapeutic method. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the methods of copending Application No. 10/772,913 to stimulate the immune system and to combine this method with radiation therapy as taught by Milas. One would have been motivated by the teachings of Milas that methods of treating cancer by immunotherapy may be enhanced by combining them with radiation therapy.

This is a provisional obviousness-type double patenting rejection.

Claims 1-7, 10, 19, and 85-87 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 4, 5, 7, 8, 10-16, 19-20, 30 and 33 of copending Application No. 10/780,114. Although the conflicting claims are not identical, they are not patentably distinct from each other because the methods claimed in 10/780,114 anticipate the methods of claims 1-7, 10, 19 and 85-87, which no longer recite a step

of administering radiation therapy. Thus, the methods of copending application 10/780,114 recite all the limitations of claims 1-7, 10, 19 and 85-87 of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 31-33, 35, 36, 40, 42, 55-68, 112-119 and 152-156 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 4, 5, 7, 8, 10-16, 19-20, 30 and 33 of copending Application No. 10/780,114 in view of Milas (Milas, L., Develop. Biol. Standard., 38: 301-306, 1978. The methods of copending Application No. 10/780,114 are drawn to method comprising administering to a mammal a cationic liposome delivery vehicle and a eukaryotic nucleic acid molecule that comprises salmon sperm and/or calf thymus DNA (which is a ligand for a pattern recognition receptor). The methods do not recite a step of administering radiation therapy. However, Milas teaches combining an immunotherapeutic method with radiation therapy to increase the effectiveness of an immunotherapeutic method. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the methods of copending Application No. 10/780,114 to stimulate the immune system and to combine this method with radiation therapy as taught by Milas. One would have been motivated by the teachings of Milas that methods of treating cancer by immunotherapy may be enhanced by combining them with radiation therapy.

This is a provisional obviousness-type double patenting rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 152-155 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 152-155 are indefinite because they depend from claim 1, which no longer recites a step of administering radiation therapy. Claims 152-155, therefore, lack antecedent basis for “the radiation therapy”.

Claim Rejections - 35 USC § 102

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-7, 10, 19, and 85-87 are rejected under 35 U.S.C. 102(e) as being anticipated by Krieg (US 2006/0089326 A1; published Apr. 27, 2006; effective filing date Oct. 30, 1996).

Claims 1-7, 10, 19, and 85-87 no longer recite a step of administering radiation therapy.

Krieg teaches a method for stimulating an immune response in a subject comprising administering to the subject a compositions comprising a nucleic acid delivery complex having a CpG containing immunostimulatory nucleic acid associated with a sterol or a lipid, where the lipid may be cationic liposome (see claim 22), where the nucleic acid is 8-100 bases in length. Thus, Krieg teaches administering at least one ligand for a pattern recognition receptor and a

delivery vehicle comprising a cationic (positively charged) liposome. Krieg's method results in the modulation of an immune response. Krieg teaches treating cancer (see claim 51). Krieg teaches treatment of cancers of the brain, lung, ovary, breast, prostate, colon, or sarcomas (see page 5-6, paragraph 0048). Therefore, Krieg teaches methods that are the same as that claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-7, 10, 31-33, 40, 42-45, 61, 64, 65, 85-87, 112, 113, 118-119, and 156 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Raz (US 6,534,062; issued Mar. 18, 2003; effective filing date is July 5, 2000) in view of Whitmore (Whitmore, M. et al. Gene Therapy, 6: 1867-1875, 1999), or Dow (Dow, S.W., et al. The Journal of Immunology, 163: 1552-1561, 1999).

Applicants assert that Raz does not teach or suggest method comprising administering a ligand for pattern recognition receptor and a delivery vehicle comprising a positively charged liposome, and that the teachings of Whitmore or Dow do not cure the defects of Raz; and that there is no motivation to combine the teachings of Raz with either Whitmore or Dow; and there is no reasonable expectation of success in arriving at methods for treating cancer by administering a ligand for a pattern recognition receptor and a delivery vehicle comprising a positively charged liposome as required by the instant claims.

Applicants' arguments have been carefully considered, but fail to persuade. Raz teaches the use of liposomes, but fails to explicitly characterize the liposomes. As taught by Whitmore or Dow, cationic liposomes were well known in the art to be used for the delivery of nucleic acids. Therefore, the motivation to use cationic liposomes is provided by the teachings of Whitmore or Dow, because Whitmore or Dow characterizes the nature of liposomes useful for the delivery of nucleic acids, and because Raz contemplates the use of liposomal delivery vehicles.

Claims 1, 31, 61 and 62 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Raz (*supra*) in view of Whitmore (*supra*), or Dow (*supra*), and further in view of Maes (US 3,725,545; issued Apr. 3, 1973 for the reasons of record).

Claims 1, 31 and 60-62 encompass methods where the ligand is an oligonucleotide that comprises at least one of poly I:C or related poly I:C oligonucleotides.

Applicants' arguments are essentially the same as presented for the rejection above: that there is no suggestion or motivation or reasonable expectation of success to combine the nucleic acids of Raz with the cationic liposomes of Whitmore or Dow, and that Maes does not cure this deficiency. Applicants' arguments have been carefully considered, but fail to persuade. Raz teaches the use of liposomes, but fails to explicitly characterize the liposomes. As taught by Whitmore or Dow, cationic liposomes were well known in the art to be used for the delivery of nucleic acids. Therefore, the motivation to use cationic liposomes is provided by the teachings of Whitmore or Dow, because Whitmore or Dow characterizes the nature of liposomes useful for the delivery of nucleic acids, and because Raz contemplates the use of liposomal delivery vehicles.

Claims 31-33, 35, 36, 40, 42, 55-68, 112-119 and 152-156 are rejected under 35 U.S.C. 103(a) as being unpatentable over Krieg (US 2006/0089326 A1; published Apr. 27, 2006; effective filing date Oct. 30, 1996) in view of Milas (*supra*).

Krieg teaches a method for stimulating an immune response in a subject comprising administering to the subject a composition comprising a nucleic acid delivery complex having a CpG containing immunostimulatory nucleic acid associated with a sterol or a lipid, where the

lipid may be cationic liposome (see claim 22), where the nucleic acid is 8-100 bases in length. Thus, Krieg teaches administering at least one ligand for a pattern recognition receptor and a delivery vehicle comprising a cationic (positively charged) liposome. Krieg's method results in the modulation of an immune response. Krieg teaches treating cancer (see claim 51). Krieg teaches treatment of cancers of the brain, lung, ovary, breast, prostate, colon, or sarcomas (see page 5-6, paragraph 0048). Krieg teaches the treatment of cancer by means of chemotherapy in combination of the method of administering immunostimulatory nucleic acids associated with a sterol or a lipid for the purpose of increasing the responsiveness to chemotherapy or immunotherapy (see page 18, paragraph 0144). Krieg does not teach combination with radiotherapy.

However, Milas teaches combining an immunotherapeutic method with radiation therapy to increase the effectiveness of an immunotherapeutic method. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the methods of Krieg to stimulate the immune system and to combine this method with radiation therapy as taught by Milas. One would have been motivated by the teachings of Milas that methods of treating cancer by immunotherapy may be enhanced by combining them with radiation therapy. One would have had a reasonable expectation of success because Milas teaches that the two therapy modalities work together to increase the effectiveness of the immunotherapeutic method.

Conclusion

No claim is allowed.

Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on 9/19/2008 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609.04(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne Holleran, whose telephone number is (571) 272-0833. The examiner can normally be reached on Monday through Friday from 9:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on (571) 272-0832. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Official Fax number for Group 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Anne L. Holleran
Patent Examiner
January 5, 2009

/Larry R. Helms/
Supervisory Patent Examiner, Art Unit 1643